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Silencing the *INK4A/ARF* locus

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The importance of the INK4A/CDKN2A locus, encoding the p16/INK4a and p19/ARF proteins, in tumor suppression is underscored by the high frequency of mutation or silencing of the locus in human tumors. In the April 24 Proceedings of the National Academy of Sciences, Magdinier and Wolffe describe the role of the methyl-CpG binding protein MBD2 in *INK4a/ARF* gene repression in cancer cells (*Proc Natl Acad Sci USA* 2001, **98:**4990-4995). They used chromatin immunoprecipitation (ChIP) experiments to study MBD2 binding to methylated CpG islands in the promoters of the *p16/INK4a* and *p19/ARF* genes in human colon carcinoma cell lines. Magdinier and Wolffe provide a mechanism for MBD2 repression in which MBD2 binding to hypermethylated *INK4a/ARF*promoters excludes the acetylated histones H3 and H4, leading to gene silencing. This effect could be overcome by combined treatment with compounds that inhibit deacetylation and methylation.

References

1. The INK4A/ARF locus and its two gene products.

2. *Proceedings of the National Academy of Sciences*, [http://www.pnas.org]

3. Identification and characterization of a family of mammalian methyl-CpG binding proteins.